

Measurement of magnetic fields and current source localization in auditory cortical activity of rats by a 12-channel dc-SQUID gradiometer

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1 Introduction

Most of the previously reported studies on the auditory brain function of small animals used invasive techniques, such as the insertion or placement of electrodes in the cortex [1]. The invasive measurement is applied to studies on short-term experiments because maintaining optimum conditions for a long period of time is difficult in small animals.

This study focused on the noninvasive measurement and localization of the auditory cortical activation in the rat brain. The weak auditory evoked magnetic fields of up to 1 pT order with a 7.5 mm spatial resolution were measured using a 12-channel high-resolution DC-SQUID magnetometer. The distribution of magnetic fields was analyzed, and the source of the auditory activity was localized by iterative minimum norm estimation (MNE) [2,3]. The global average and the histogram of the current sources were calculated statistically.

2 Experimental design

Rat brain activities were measured using a 12-channel SQUID gradiometer in a magnetically shielded room (2.52 m length, 2.52 m width, 2.49 m height). Twelve pickup coils were located on a 7.5 mm grid. The pickup coil was a first order gradiometer, which had a 5 mm diameter and a 15 mm baseline. The distance between the pickup coil and the bottom of the dewar was 5 mm. The sensitivity error of each pickup coil was less than 5 percent for the phantom experiment. Calibration of sensitivity was performed. A magnetically shielded room consisting of five 1 mm-thick layers of permalloy and one 0.035 mm thick layer of copper was used. The field sensitivity was 100 fT/√Hz in the white noise frequency range.

The measured magnetic fields were filtered from 1 Hz to 100 Hz. Averaging of the magnetic fields was performed for over 3000 auditory stimuli. The center of the base of the dewar was placed on the right ear of the rat. Figure 1 shows the positions between 12 pickup coils located on the top of the

rat's head. The base of the dewar was positioned close on the rat's head. The origin was defined as the intersection between the median plane and the coronal plane through both ears on the scalp.

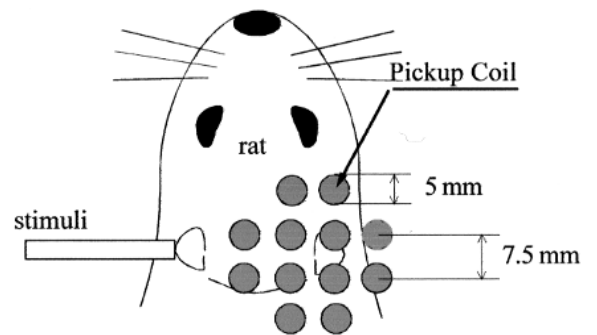


Figure 1: Positions of 12 pick-up coils on the rat's head. Rat received stimulus to the left ear and responses were measured from the right side of the head.

3 Subject and auditory stimulation

The auditory evoked magnetic fields in eight male rats were measured. The rats, averaging 333 g (SD = 222 g), were anesthetized intraperitoneally with Urethane (1g/kg) and measured with fixed limbs and heads.

The left ear of each rat was stimulated with tone bursts of 3 kHz, 10 ms in duration and 85 dB in amplitude at the rat's ear. The stimuli were presented at 2 Hz through two meters of plastic tubing with an inner diameter of 4 mm.

4 Analysis

The primary current sources in the rat's cortex were localized by iterative MNE. The negative aspect of MNE is that the localization of sources is inaccurate. We added the iterative algorithm to MNE to improve the localization. Magnetic fields $B = [b_1, b_2, \dots, b_M]^T$ are linearly related to the dipolar primary current distribution $Q = [q_1, q_2, \dots, q_N]^T$, where M is the number of sensors and N is the number of current source locations;

$$B = LQ \quad (1)$$

where L is the lead field, B is determined from the magnetic fields, which were detected by 12 magnetometers. The conventional method can be written as follows:

$$Q = \Gamma^{-1}BL \quad (2)$$

where

$$\Gamma = LL^T \quad (3)$$

In practice, to decrease the numerical instability from noise, small eigenvalues of Γ were ignored. The cutoff value was defined as K ($K < M$).

A model of the rat's brain was reconstructed using 172 grid units by examining the photos of the sliced tissues and the magnetic resonance images of the rat's brain. The reconstructed rat brain and the three axes are shown in Figure 2. The 172 grid units represent the locations on the rat's cortex. The left side indicates the anterior cortex and the right side indicates the posterior cortex.

To ensure accuracy of the estimated current sources, the reconstructed magnetic fields (bc) were calculated by the estimated current sources. The correlation coefficient C was calculated as follows:

$$C = \frac{\sum_{i=1}^M (b_i - \bar{b})(bc_i - \bar{bc})}{\sqrt{\sum_{i=1}^M (b_i - \bar{b})^2} \sqrt{\sum_{i=1}^M (bc_i - \bar{bc})^2}} \quad (4)$$

where $\bar{b}$ and $\bar{bc}$ are averages of b_i and bc_i ($i = 1 \dots M$).

In the iterative algorithm, reconstruction points in the low amplitude currents were deleted when the correlation coefficient was lower than 0.9.

The direction of the localized current sources consists of the x component and y component because the z component of magnetic fields on the plane was measured.

In the statistical analysis, the global average and the histogram of the current sources were calculated.

5 Results

Figure 3 shows 12 auditory evoked magnetic fields and highlighted waveforms of a rat. The intersection between the vertical line and the horizontal line indicates the point of stimulus onset. The auditory evoked magnetic fields of the rat consisted of biphasic waves with latencies of 73.1 ms and 91.0 ms. The average latency of the auditory evoked magnetic fields in the eight rats was 53.8 ms ($SD=9.9$ ms) and the average amplitude was 1.7 pT ($SD = 1.2$ pT).

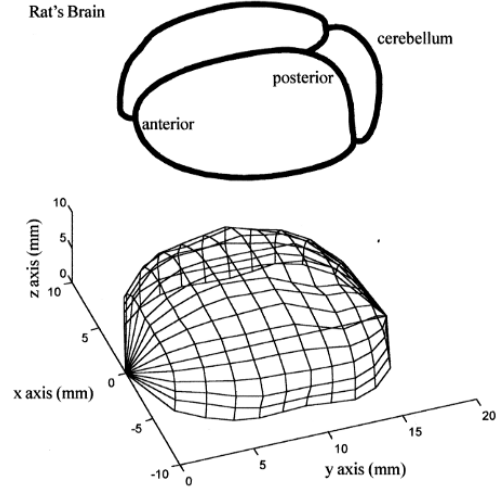


Figure 2: Reconstructed rat brain and the three axes. A model of the rat's brain reconstructed into 172 grid units based on the photos of the tissue slices and the magnetic resonance images of the rat's brain. The 172 grid units represent the locations on the rat's cortex. The left side indicates the anterior cortex and the right side indicates the posterior cortex.

Figure 4 shows the localized distribution of the current sources on the right hemisphere of the rat's cortex by iterative MNE. The right side indicates the anterior cortex and the left side indicates the posterior cortex. The arrows represent the estimated currents. The maximum arrow was localized at the left temporal cortex, where the amplitude was 2.5 nAm, and the direction of the maximum current was to the left anterior. The correlation coefficient was 0.92.

Figure 5 shows the global average of the estimated current sources of eight rats. The maximum current was localized at the left temporal cortex and flowed to the left anterior. The weak currents, however, were estimated at the area besides the auditory cortex.

Figure 6 shows the histogram of the current sources by iterative MNE in 8 rats. The positional overlap of the main estimated current sources, whose amplitudes were more than 0.8 of the maximum, in rats were counted by identical grid units. The size of the circles indicate the percentage of reproducibility. The highest percentage of reproducibility of the estimated current sources in eight rats was identified at the left temporal cortex (62.5%).

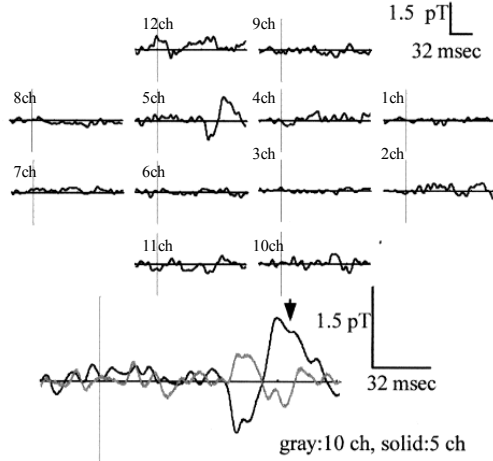


Figure 3: 12 auditory evoked magnetic fields and highlighted waveforms of a rat. The intersection between the vertical line and the horizontal line indicates the stimulus-onset. Arrow equals 91msec

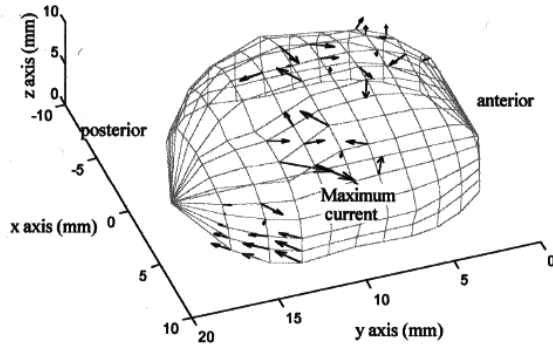


Figure 4: The localized distribution of the current sources on the rat cortex by iterative MNE. This is a view of the right hemisphere in the rat's cortex. The right side indicates the anterior cortex and the left side indicates the posterior cortex. The arrows represent the estimated currents. The maximum current was localized at the left temporal cortex, the amplitude is 2.5 nAm, the direction of the maximum current was to the left anterior.

5 Discussion

In this study, the biphasic waves of auditory evoked magnetic fields were measured noninvasively and current sources were localized at the right temporal cortex. Barth et al. [1] reported that four peaks (P1, P2, N1 and N2) appeared on the auditory evoked potential. The responses were measured in auditory areas (rostral-lateral subdivision and caudal-lateral subdivision). In our studies, magnetic fields of the N2 component were successfully measured.

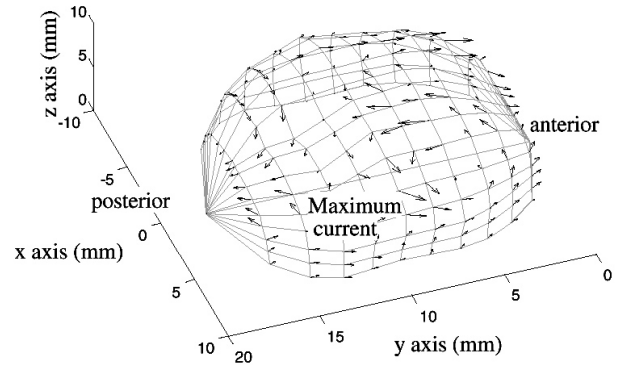


Figure 5: The global average of the estimated current sources of eight rats. The maximum current was localized at the left temporal cortex and flowed to left anterior.

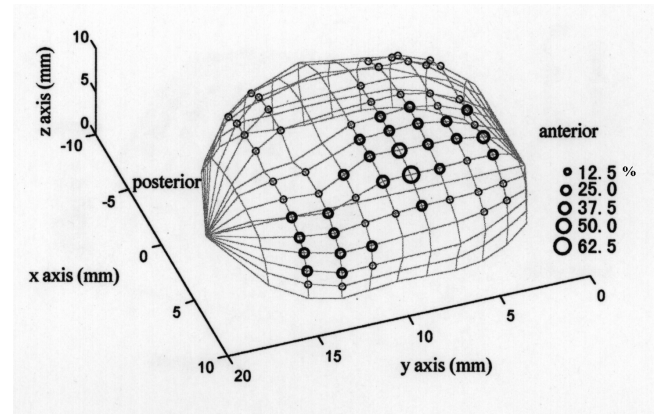


Figure 6: The histogram of the current sources by iterative MNE in 8 rats. The positional overlap of estimated current sources in rats were counted each grids. The size of the circle indicates the percentage of frequency.

The weak currents were estimated at the area besides the auditory cortex. We assumed that the weak currents were produced by the contralateral response of the auditory cortex and the noise of the estimation.

The positive application of our system requires further research on the safety of brain magnetic stimulation for long term studies [4]. Noninvasive measurement by our system is useful for *in vivo* studies under identical environmental parameters.

Acknowledgement

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References

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